

**Remarks**

**Species Election**

Applicant herewith confirms election of monoclonal antibody species SNj6 of claim 4 provisionally elected by telephone on March 9, 2005.

**Information Disclosure Statement**

In respect of the listing of references in the specification, relevant references of which Applicant is aware were listed on the Information Disclosure Statement mailed October 21, 2004.

**Objection to Specification**

The Examiner has objected to the specification and asserted that page 4, lines 30+ appear to describe details of Figure 7, but a comparison with Figure 7 does not appear to coincide. The Examiner has queried what the eight lines in the Figure represent. Applicant points out that, on page 15, lines 16-21, it is indicated that chimeras with established tumors were distributed into four groups (n = 8 for each group) and the individual groups were treated to generate the results presented in Fig. 6. On page 17, lines 10-11, it is indicated that the therapeutic effect on individual chimeras in each group of Fig. 6 is presented in Fig. 7. In Fig. 7, it is indicated that "n=8." Thus, it is clear from the specification that each of the eight lines of Fig. 7 represents tumor size of each of the eight mice of the groups set forth in Fig. 6. Applicant therefore respectfully requests the Examiner to remove the stated objection.

**Claim Rejections - 35 USC §112**

The Examiner has rejected claims 1-13 as lacking enablement. However, the Examiner has acknowledged that the present specification discloses a synergistic relationship between the combination of anti-endoglin SNj6 and cyclophosphamide (CPA) or doxorubicin. In this regard, claims 1, 6, 7, 9 and 10 have been amended to specify that the anti-endoglin antibody is

SN6j and that SN6j is used in combination with CPA or doxorubicin to obtain a synergistic effect on the inhibition of tumor growth. Additionally, claims 2, 3, 4 and 8 have been canceled. In view of these amendments, removal of the stated rejection is respectfully requested.

The Examiner has also argued that, in order for immunotherapy to be effective, there needs to be a correlation between expression of endoglin (EDG) in normal versus tumor tissues, but an article by the present inventor indicates EDG is not a tumor specific marker and that it is expressed in varying degrees in the vasculature of normal tissues (Int. J. Cancer (2002); 99:310-311; page 310, 2<sup>nd</sup> column, 1<sup>st</sup> paragraph). However, Applicant respectfully points out that the this same reference, in the same paragraph, states that: "Despite this limitation, we could effectively target tumor-associated vasculature using select anti-EDG MAbs and immunoconjugates." Further, it is also stated in the same paragraph that "the rapidly dividing endothelial cells of tumor vasculature are much more susceptible to killing by anti-EDG MAbs than the quiescent vascular endothelium of normal tissues." Thus, Applicant submits there is a correlation between expression of EDG in normal versus tumor tissues and that this correlation would enable one to practice the claimed method without undue experimentation. The Examiner is therefore respectfully requested to remove the stated rejections.

**Claim Rejections - 35 USC §102**

**Claims 1, 2, 4, and 6-9 under 35 USC 102(a)**

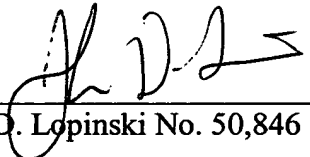
Claims 1, 2, 4, and 6-9 were rejected as being anticipated by Takahashi et al., (Cancer Research, 2001, 61:7846-7854). Applicant has herewith provided a Rule 1.132 Declaration indicating that this reference is the inventor's own work and that all authors listed on this reference who are not named inventors on the instant application were working under the inventor's direction and did not make inventive contribution to the present application. Applicant accordingly requests the Examiner to remove the stated rejection.

**Conclusion**

Based on the above arguments and amendments, Applicants believe that claims 1, 5-7, and 9-13 are now in a condition for allowance and therefore respectfully request the Examiner to allow these claims.

This application is being filed within 3 months of the date of the office action and therefore it is believed that no fee is due. If however, that is incorrect, any fee due may be charged to Deposit Account No. 08-2442.

Respectfully submitted,  
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Dated: July 18, 2005